REMARKS

Claims 1-4, 7-8 and 10-13 are rejected under 35 USC 103(a) as being unpatentable over Seo et al., WO 03/033593 in view of Li et all, Polymer, 39, pp. 4421-4427 (1998) for the reasons set forth in the previous Office Action dated July 17, 2009. Claims 1-5 and 7-134 are rejected under 35 USC 1034(a) as being unpatentable over Seo et al., in view of Li et all. in view of Sodergard, US 2004/0091573. These rejections are respectfully traversed.

The present invention relates to the solubilization of poorly water-soluble drugs by entrapping the drugs in micelles. When forming micelles, a linear polylactic acid salt such as that disclosed in the Seo reference is restricted to have a molecular weight of 2000 Daltons or less because of the water solubility. Thus, if such a polymer having a molecular weight of 2000 Daltons or more is used to form micelles trapping a drug, the drug cannot be maintained in the micelles for a long period of time because of poor solubility. The present invention stabilizes micelles by increasing the molecular weight of the polymer which is used to form the micelles and accordingly by lowering the critical micelle concentration (CMC). If the CMC is high, more polymer is required to form micelles and then the micelles become unstable, which results in a precipitation of the poorly water-soluble drugs. If the molecular weight of a linear polylactic acid salt is increased, it becomes more difficult to dissolve in water. The present invention utilizes a multi-arm (branched) polymer structure wherein the total molecular weight increases but that of each polylactic acid arm does not, while maintaining the water solubility.

The Seo reference does not provide any teaching or suggestion as to whether the molecular weight of a linear polylactic acid salt should increase, how to increase the molecular weight and whether the water solubility would be maintained and micelles could be formed even if the molecular weight is increased.

The Li reference relates to the conversion of a linear ABA tri-block copolymer to a star-block PLLG-PEO copolymer having stearic architecture and a shorter PLLG block. The Li reference discloses that the star-block copolymer shows slow mass erosion because of slower

cleavage of the PEO-PLLG block (please see page 4426, Fig. 6). Therefore, the effect of Li's star-block copolymer is considered to come from the PEO-PLLG bond showing slower cleavage.

The purpose of the Li reference is to delivery proteins. It's polymer, which is not dissolved in water, is a block copolymer comprising PEG (polyethylene glycol). This is clearly distinguishable from the present polylactic acid derivatives. Furthermore, the Li reference provides no teaching or suggestion as to how to maintain the water solubility of a polymer when its molecular weight increases. Thus, the Li reference has no relationship at all to entrapping poorly water-soluble drugs in micelles.

The present invention, on the other hand, does not relate to block copolymers comprising PEG. Therefore, from the PEO-PLLG bond showing slower cleavage in the Seo reference, one skilled in the art would not expect that the multi-arm polymer structure of the present invention would also have such an effect. The concept of the present invention focuses on the fact that the equilibrium rate of micelles having dynamic behavior (micelles are in equilibrium with corresponding unimers) become slower by increasing the molecular weight of the polymer constituting the micelles, and thus the solubility of the micelles is improved. This concept of the present invention cannot be found in either the Seo or Li references and accordingly the prior art references do not teach or suggest the improvement in micelle stability while maintaining water solubility by increasing the molecular weight of polymer arms in a multi-arm polymer structure.

In rejecting the claims of the present application, the Examiner considers PEG (polyethylene glycol) as being equivalent to ethylene glycol. However, polyethylene glycol is a polymer whereas ethylene glycol is a monomer. The Examiner argues that since the polyethylene glycol content is 14 to 33%, Li's polymer may also form a small core. However, in the case of the polyethylene glycol content of 14%, since the polymer weight of four (4) PEO arms is 7100 Daltons, each branch of PEO has a molecular weight of about 1800 Daltons. That is, in this case, the polymer has four (4) PEO chains with 1800 Daltons which are arranged in a star-like shape. Such a structure is significantly different from that of the present polymer wherein ethylene glycol with a molecular weight of 62 is present in the inner part. The Examiner

appears to believe that Li's polymer has the same micelle-forming properties as the present invention. However, Li's polymer merely swells in water and is not dissolved and thus cannot form micelles (please see page 4426).

In rejecting claims 1-5 and 7-13, the Examiner recognizes that neither the Seo or Li references discloses the specific polyol cores as recited in dependent claims 5 and 9. Accordingly, the Examiner has further relied upon the Sodergard reference to fill this deficiency.

The Sodergard reference is directed to a chewing gum. In the Sodergard reference, biodegradable polymers are used as a gum base. Clearly, the technical field to which the Sodergard reference is directed, is totally different from that of the present invention, which is directed to a drug delivery formulation. In the Sodergard reference, it is not necessary for the polymer to entrap drugs therein, at all. In addition, the polymer utilized in the Sodergard reference is used for a gum base and thus should not, in fact, be water soluble. Because of the substantial difference between the technology of the Sodegard reference and that of the Seo and Li references as well as the present invention, one skilled in the art would certainly not contemplate combining the references as suggested by the Examiner without completely reconstructing the teachings of the references in view of the Applicants' own disclosure. Even if, for sake of argument, it would be possible to combine the references as suggested by the Examiner, said combination would still not reach the Applicants' inventive contribution which is concerned with the improvement of micelle stability while maintaining water solubility by increasing the molecular weight of polymer arms in a multi-arm polymer structure.

In the Examiner's Office Action the Examiner has indicated that the future of entrapping drugs for a long time is not recited in the claims. It is the Applicants' position that such a feature is obtained from the specific structure and molecular weight as presently recited in amended claims 1 and 7 of the present application. In any event, claim 14 has been added to the present application to specifically refer to this aspect of the present invention.

Accordingly, in view of the above amendments and remarks reconsideration of the rejections and allowance of all of the claims of the present application are respectfully requested. In the event that the proposed Amendment does not place the present application into condition for allowance, entry thereof is respectfully requested as placing the present application into better condition for appeal.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Joseph A. Kolasch, Registration No. 22463 at the telephone number of the undersigned below to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Director is hereby authorized in this, concurrent, and future replies to charge any fees required during the pendency of the above-identified application or credit any overpayment to Deposit Account No. 02-2448.

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Respectfully submitted,

By _____
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